

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/003982

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61K39/395 A61K38/00 A61K45/00 A61P37/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHEDMinimum documentation searched (classification system followed by classification symbols)
 IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|--|-----------------------|
| P, X | <p>KATZAV SHULAMIT: "Vav 1: an oncogene that regulates specific transcriptional activation of T cells" BLOOD, vol. 103, no. 7, 1 April 2004 (2004-04-01), pages 2443-2451, XP002293398 ISSN: 0006-4971 abstract page 2443, left-hand column, paragraph 1 page 2444, right-hand column, paragraph 2 page 2445, left-hand column, paragraph 2 - page 2446, left-hand column, last paragraph page 2449 Citation 51</p> <p>-----</p> <p style="text-align: center;">-/-</p> | 1-8, 10 |

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the International filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the International filing date but later than the priority date claimed

- *T* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the International search

20 August 2004

Date of mailing of the International search report

02/09/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Hars, J

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|--|-----------------------|
| X | TURNER MARTIN ET AL: "VAV proteins as signal integrators for multi-subunit immune-recognition receptors." NATURE REVIEWS IMMUNOLOGY, vol. 2, no. 7, July 2002 (2002-07), pages 476-486, XP009035501 ISSN: 1474-1733 cited in the application | 5-8 |
| A | abstract page 476, right-hand column - page 477, left-hand column page 482, left-hand column, paragraphs 3,5 table 1 Citation 84 | 1-4,10 |
| A | SCHUEBEL KORNEL E ET AL: "Phosphorylation-dependent and constitutive activation of Rho proteins by wild-type and oncogenic Vav-2" EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 17, no. 22, 16 November 1998 (1998-11-16), pages 6608-6621, XP001183075 ISSN: 0261-4189 abstract page 6611, left-hand column | 1-4,10 |
| A | KAMINUMA OSAMU ET AL: "Vav-Rac1-mediated activation of the c-Jun N-terminal kinase/c-Jun/AP-1 pathway plays a major role in stimulation of the distal NFAT site in the interleukin-2 gene promoter" MOLECULAR AND CELLULAR BIOLOGY, vol. 21, no. 9, May 2001 (2001-05), pages 3126-3136, XP002293400 ISSN: 0270-7306 abstract | 1-4,10 |
| A | GERMANI ANTONIA ET AL: "hSiah2 is a new Vav binding protein which inhibits Vav-mediated signaling pathways" MOLECULAR AND CELLULAR BIOLOGY, vol. 19, no. 5, May 1999 (1999-05), pages 3798-3807, XP002293401 ISSN: 0270-7306 abstract page 3798, left-hand column - page 3799, left-hand column, paragraph 2 page 3799, left-hand column, last paragraph | 1-4,10 |
| | ----- -/- | |

INTERNATIONAL SEARCH REPORTInternational Application No
PCT/EP2004/003982**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|--|-----------------------|
| A | ABBAS, ABUL K.: "CELLULAR AND MOLECULAR IMMUNOLOGY" 31 December 1997 (1997-12-31), W.B. SAUNDERS , PHILADELPHIA, USA , XP002293402 page 166, right-hand column, paragraph 1 ----- | 1-4, 10 |

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-3 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: 1-4, 9, 10 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 1-3 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box II.2

Claims Nos.: 1-4,9,10

Present claims 1-4,9,10 relate to a substance defined by reference to a desirable characteristic or property, namely to be an inhibitor of Vav protein, useful in the treatment of several diseases.

The claims cover all substances having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such substances. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the substance by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to antibodies or antibody fragments against Vav-1 protein, useful in the treatment of graft rejection, as disclosed in the description on page 2, last paragraph to page 4, third paragraph.

Claim 9 relating to substances obtainable through the screening method has not been searched at all.

Idem for subject matter of claims 1-4,9,10 relating to Vav protein in general or Vav-2 protein in particular, and for diseases other than graft rejection.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.